

AMENDMENT

In the Claims:

Please amend claims 31 and 34-63 as follows:

31. (Twice Amended) An isolated nucleic acid molecule encoding a human Fab molecule, comprising:

a first nucleotide sequence encoding a first polypeptide that is homologous to the binding portion of a $\gamma 1$ heavy chain variable region (V_H) of said human Fab molecule where said heavy chain region exhibits immunological binding affinity for a hepatitis C virus (HCV) E2 antigen; and wherein the first nucleotide sequence is selected from the group consisting of the contiguous sequence of depicted in Figure 4A (SEQ ID NO:22) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4B (SEQ ID NO:23) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4C (SEQ ID NO:24) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4D (SEQ ID NO:25) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4E (SEQ ID NO:19) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4F (SEQ ID NO:26) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; and the contiguous sequence of depicted in Figure 4G (SEQ ID NO:27) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; and

a second nucleotide sequence encoding a second polypeptide that is homologous to the binding portion of a κ light chain variable region (V_L) of said human Fab molecule where said light chain variable region exhibits immunological binding affinity for a hepatitis C virus (HCV) E2 antigen, and wherein the second nucleotide sequence is selected from the group consisting of the contiguous sequence of depicted in Figure 3A

(SEQ ID NO:15) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3B (SEQ ID NO:16) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3C (SEQ ID NO:17) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3D (SEQ ID NO:18) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3E (SEQ ID NO:19) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3F (SEQ ID NO:20) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; and the contiguous sequence of depicted in Figure 3G (SEQ ID NO:21) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto, and wherein said Fab molecules have binding affinity greater than $1 \times 10^7 \text{ M}^{-1}$ for HCV E2.

34. (Amended) The nucleic acid molecule of claim 31, wherein the first nucleotide sequence is depicted in Figure 4A (SEQ ID NO:22).

35. (Amended) The nucleic acid molecule of claim 31, wherein the first nucleotide sequence is depicted in Figure 4B (SEQ ID NO:23).

36. (Amended) The nucleic acid molecule of claim 31, wherein the first nucleotide sequence is depicted in Figure 4C (SEQ ID NO:24).

37. (Amended) The nucleic acid molecule of claim 31, wherein the first nucleotide sequence is depicted in Figure 4D (SEQ ID NO:25).

38. (Amended) The nucleic acid molecule of claim 31, wherein the first nucleotide sequence is depicted in Figure 4E (SEQ ID NO:19).

39. (Amended) The nucleic acid molecule of claim 31, wherein the first nucleotide sequence is depicted in Figure 4F (SEQ ID NO:26).

40. (Amended) The nucleic acid molecule of claim 31, wherein the first nucleotide sequence is depicted in Figure 4G (SEQ ID NO:27).

41. (Amended) The nucleic acid molecule of claim 31, wherein the second nucleotide sequence is depicted in Figure 3A (SEQ ID NO:15).

42. (Amended) The nucleic acid molecule of claim 31, wherein the second nucleotide sequence is depicted in Figure 3B (SEQ ID NO:16).

43. (Amended) The nucleic acid molecule of claim 31, wherein the second nucleotide sequence is depicted in Figure 3C (SEQ ID NO:17).

44. (Amended) The nucleic acid molecule of claim 31, wherein the second nucleotide sequence is depicted in Figure 3D (SEQ ID NO:18).

45. (Amended) The nucleic acid molecule of claim 31, wherein the second nucleotide sequence is depicted Figure 3E (SEQ ID NO:19).

46. (Amended) The nucleic acid molecule of claim 31, wherein the second nucleotide sequence is depicted in Figure 3F (SEQ ID NO:20).

47. (Amended) The nucleic acid molecule of claim 31, wherein the second nucleotide sequence is depicted in Figure 3G (SEQ ID NO:21).

48. (Twice Amended) An isolated nucleic acid molecule, comprising a first nucleotide sequence encoding a binding portion of a $\gamma 1$ heavy chain variable region (V_H) of a human Fab molecule obtained from a combinatorial library, wherein said Fab molecule exhibits immunological binding affinity greater than $1 \times 10^7 M^{-1}$ for a hepatitis C virus (HCV) E2 antigen and further wherein the first nucleotide sequence is selected from the group consisting of the contiguous sequence of depicted in Figure 4A (SEQ ID NO:22) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the

contiguous sequence of depicted in Figure 4B (SEQ ID NO:23) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4C (SEQ ID NO:24) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4D (SEQ ID NO:25) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4E (SEQ ID NO:19) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 4F (SEQ ID NO:26) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; and the contiguous sequence of depicted in Figure 4G (SEQ ID NO:27) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto.

49. (Amended) The nucleic acid molecule of claim 48, wherein the first nucleotide sequence is depicted in Figure 4A (SEQ ID NO:22).

50. (Amended) The nucleic acid molecule of claim 48, wherein the first nucleotide sequence is depicted in Figure 4B (SEQ ID NO:23).

51. (Amended) The nucleic acid molecule of claim 48, wherein the first nucleotide sequence is depicted in Figure 4C (SEQ ID NO:24).

52. (Amended) The nucleic acid molecule of claim 48, wherein the first nucleotide sequence is depicted in Figure 4D (SEQ ID NO:25).

53. (Amended) The nucleic acid molecule of claim 48, wherein the first nucleotide sequence is depicted in Figure 4E (SEQ ID NO:19).

54. (Amended) The nucleic acid molecule of claim 48, wherein the first nucleotide sequence is depicted in Figure 4F (SEQ ID NO:26).

55. (Amended) The nucleic acid molecule of claim 48, wherein the first

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A nucleotide sequence is depicted in Figure 4G (SEQ ID NO:27).

56. (Twice Amended) An isolated nucleic acid molecule, comprising a first nucleotide sequence encoding a binding portion of a κ light chain variable region (V_L) of a human Fab molecule obtained from a combinatorial library, wherein said Fab molecule exhibits immunological binding affinity greater than $1 \times 10^7 \text{ M}^{-1}$ for a hepatitis C virus (HCV) E2 antigen and further wherein the first nucleotide sequence is selected from the group consisting of the contiguous sequence of depicted in Figure 3A (SEQ ID NO:15) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3B (SEQ ID NO:16) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3C (SEQ ID NO:17) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3D (SEQ ID NO:18) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3E (SEQ ID NO:19) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; the contiguous sequence of depicted in Figure 3F (SEQ ID NO:20) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto; and the contiguous sequence of depicted in Figure 3G (SEQ ID NO:21) or a contiguous sequence of nucleotides with at least 90% sequence identity thereto.

57. (Amended) The nucleic acid molecule of claim 56, wherein the second nucleotide sequence depicted in Figure 3A (SEQ ID NO:15).

58. (Amended) The nucleic acid molecule of claim 56, wherein the second nucleotide sequence is depicted in Figure 3B (SEQ ID NO:16).

59. (Amended) The nucleic acid molecule of claim 56, wherein the second nucleotide sequence is depicted in Figure 3C (SEQ ID NO:17).

60. (Amended) The nucleic acid molecule of claim 56, wherein the second

nucleotide sequence is depicted in Figure 3D (SEQ ID NO:18).

61. (Amended) The nucleic acid molecule of claim 56, wherein the second nucleotide sequence is depicted in Figure 3E (SEQ ID NO:19).

62. (Amended) The nucleic acid molecule of claim 56, wherein the second nucleotide sequence is depicted in Figure 3F (SEQ ID NO:20).

63. (Amended) The nucleic acid molecule of claim 56, wherein the second nucleotide sequence is depicted in Figure 3G (SEQ ID NO:21).

Please add new claims 117 to 127 as follows:

117. (New) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1A (SEQ ID NO: 1) and the contiguous sequence of amino acids depicted in Figure 2A (SEQ ID NO: 5).

118. (New) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1B (SEQ ID NO: 2) and the contiguous sequence of amino acids depicted in Figure 2B (SEQ ID NO: 6).

119. (New) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1C (SEQ ID NO: 3) and the contiguous sequence of amino acids depicted in Figure 2C (SEQ ID NO: 7).

120. (New) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1D (SEQ ID NO: 4) and the

contiguous sequence of amino acids depicted in Figure 2D (SEQ ID NO: 8).

121. (New) An isolated nucleic acid molecule that encodes a recombinant human monoclonal antibody that exhibits immunological binding affinity for a hepatitis C virus (HCV) E2 antigen, wherein the antibody comprises at least one group of three complementarity determining regions (CDRs) interposed between framework regions (FRs) said FRs derived from a human immunoglobulin, wherein the group of three CDRs is selected from the group consisting of amino acid residue numbers 32-36, 51-71, 104-121 of SEQ ID NO:1; amino acid residue numbers 32-36, 51-67, 100-116 of SEQ ID NO:2; amino acid residue numbers 32-36, 51-67, 100-117 of SEQ ID NO:3; amino acid residue numbers 31-35, 50-66, 99-114 of SEQ ID NO:4; amino acid residue numbers 23-34, 49-56, 89-97 of SEQ ID NO:5; amino acid residue numbers 23-33, 49-55, 88-95 of SEQ ID NO:6; amino acid residue numbers 23-34, 50-56, 89-97 of SEQ ID NO:7; and amino acid residue numbers 23-33, 49-55, 88-96 of SEQ ID NO:8.

122. (New) The isolated nucleic acid molecule of claim 121, wherein the antibody encoded by the nucleic acid molecule comprises a first group of CDRs with amino acid residue numbers 32-36, 51-71, 104-121 of SEQ ID NO:1 interposed between FRs, and a second group of CDRs with amino acid residue numbers 23-34, 49-56, 89-97 of SEQ ID NO:5, interposed between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

123. (New) The isolated nucleic acid molecule of claim 121, wherein the antibody comprises a first group of CDRs with amino acid residue numbers 32-36, 51-67, 100-116 of SEQ ID NO:2 interposed between FRs, and a second group of CDRs with amino acid residue numbers 23-33, 49-55, 88-95 of SEQ ID NO:6, interposed between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

124. (New) The isolated nucleic acid molecule of claim 121, wherein the antibody comprises a first group of CDRs with amino acid residue numbers 32-36, 51-67,

100-117 of SEQ ID NO:3 interposed between FRs, and a second group of CDRs with amino acid residue numbers amino acid residue numbers 23-34, 50-56, 89-97 of SEQ ID NO:7 interposed between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

125. (New) The isolated nucleic acid molecule of claim 121, wherein the antibody comprises a first group of CDRs with amino acid residue numbers amino acid residue numbers 31-35, 50-66, 99-114 of SEQ ID NO:4 interposed between FRs, and a second group of CDRs with amino acid residue numbers 23-33, 49-55, 88-96 of SEQ ID NO:8 interposed between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

126. (New) A method for providing an antibody titer to HCV in a mammalian subject, comprising introducing a therapeutically effective amount of a composition comprising the isolated nucleic acid of claim 120 to said subject.

127. (New) A method for providing an antibody titer to HCV in a mammalian subject, comprising introducing a therapeutically effective amount of a composition comprising the isolated nucleic acid of claim 121 to said subject.